Please cancel claims 3, 10 and 50 to 52.

New claim 53 has been added.

Also submitted herewith are "Clean Claim Sheets" with the claims as pending after entry of the present amendments.

REMARKS

Applicants note that the Office Action mailed April 25, 2002 set an initial three (3) month shortened statutory period for response. Applicants note that submitted herewith is a Petition under 37 C.F.R. § 1.136(a) for an one-month extension of time and a check which includes the required fee. With the granting of this Petition, the time period in which to submit a timely response to the Office Action mailed April 25, 2002 will be extended to August 25, 2002.

Amendments to the Claims

Claims 1, 4, 7, 8, 11, 12, 13 and 14 have been amended and claims 3, 10 and 50 to 52 have been cancelled. Applicants reserve their right to pursue subject matter deleted from the amended claims and of the cancelled claims, to the extent that is not covered by the pending claims after entry of the present amendments, in continuing and/or divisional applications as appropriate.

Claims 1, 7, 8, 12 and 14 have been amended to more particularly point out and distinctly claim the compounds and compositions of elected invention of Group I and to delete subject matter directed to nonelected inventions. Applicants reserve their rights to file continuing and/or divisional applications as appropriate, directed to the subject matter of the nonelected inventions. Claims 1 and 8 have also been amended to insert "or pharmaceutically acceptable salt or

prodrug thereof." See, e.g. the specification at page 5, line 23 and page 13, line 3.

Claims 4 and 11 which were dependent on cancelled claims 3 and 10, respectively, have been amended to be dependent on claims 2 and 9, respectively. Claim 13 has been amended to revise its dependency.

Claims 3, 10 and 50 to 52 have been cancelled without prejudice to expedite prosecution. Applicants reserve their right to pursue the subject matter of the cancelled claims in continuing and/or divisional applications as appropriate.

New claim 53 has been added. *See, inter alia*, the specification at page 17, lines 20 to 32.

Applicants submit that these amendments are clearly supported by the specification and claims, as filed, and give rise to no issue of new matter.

Applicants submit that claims 1, 2, 4 to 9, and 11 to 49 and 53, the claims which are presently pending after entry of the above-noted amendments are readable on the elected invention of Group I.

The Section 112, Second Paragraph Rejection of Paragraph 2, pages 2 to 4

Claims 1 to 5, 6 to 7, 8 to 14, 15 to 35, 36 to 49 and 50 to 52 stand rejected under 35 U.S.C. § 112, second paragraph. Applicants note that Claims 3 and 10 and 50 to 52 have been cancelled.

This rejection is respectfully traversed. Applicants submit that Claims 1, 2, 4, 5, 6 to 7, 8, 9, 11 to 14, 15 to 35, and 36 to 49 as pending after entry of the present amendments, clearly comply with the second paragraph of Section 112.

Claims 1, 8 and 14 are independent. Claims 2, 4 to 7 and 15 to 49 are dependent or ultimately dependent on claim 1. Claims 9 and 11 to 13 are dependent on claim 8.

Subparagraph A

The Examiner appears to object to the terms "aryl, aralkyl, heteroaralkyl and heteroaryl" as used for R, Ar_1 and Ar_2.

Applicants submit that the terms "aryl," "aralkyl," "heteroaryl" and "heteroaralkyl" are terms conventionally used in the art and their meanings are known to those of skill in the art. Applicants note that they have incorporated definitions of those terms in the specification, but submit the definitions represent conventional meanings for those terms. Applicants note that as part of the definitions for the terms "aralkyl", "heteroaralkyl", "aryl" and "heteroaryl", they list certain groups as "examples" or "representative examples." Applicants note that in the case of the terms "aryl" and "heteroaryl", certain groups are said to be preferred. Applicants submit that certain of the dependent claims are directed to compounds having some of the "aryl" groups which are said to be preferred. See, e.g. claims 4 to 7, 11 and 12.

Applicants do not understand the Examiner's comment:

> "The term "heteroaryl" as defined on page 11 line 20 includes aromatic C2-6 cyclic groups containing O, S, or up to four N atoms, or combination of one O or S atom with up to two N atoms. It is difficult to read C2 or C3-C4 aromatic cyclic rings having different heteroatoms."

Office Action mailed April 25, 2002 at page 3. Applicants note that known C_2, C_3 and C_4 heteroaryl compounds having different

a

heteroatoms include oxadiazole, oxazolidine, oxazole, thiazole, thiazine and the like.

Applicants do not understand the Examiner's comments with regard to "critical limitations" in the present context. Applicants note that the Examiner appears to assert that the presence of definitions for the chemical terms noted above in the specification represented "critical limitations from the specification" that he asserted "cannot be read into the claims." Applicants submit that the Examiner's reliance on In re Van Geuns 26 U.S.P.Q. 2d (BNA) 1057 (Fed Cir. 1991), is misplaced. The issues discussed and decided in that case were different.[1]

Subparagraph B

The Examiner queried regarding the recitation of "X" at page 12, line 24. The inclusion of "X" at that location appears to be a typographical error.

Applicants note that the specification has been amended at page 12, line 24 to delete "X."

Subparagraph C

Applicants note Claims 1 and 8 have been amended to insert "or a pharmaceutically acceptable salt or prodrug thereof".

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[1] In re Van Geuns dealt with a patent interference. Van Geuns argued that a particular term should be interpreted in light of the specification to include a limitation not in the claim in order to overcome an art (obviousness) rejection. The Federal Circuit noted that Van Geuns could not read a limitation into the claim at issue in order to overcome the obviousness rejection. The holding of In re Van Geuns is not applicable to the present situation.

Subparagraph D

Applicants note the Examiner's query regarding "ester or prodrug" in claim 14 and his reference to page 29, lines 4 to 5 of the specification which mentions "resolution of compounds by formation of esters or amides."

Applicants note that the reference to "esters" at page 29, lines 4 to 5, refers to synthesis procedures which include the step of formation of diastereomeric esters or amides followed by chromatographic separation as part of a procedure to resolve (or separate) stereoisomer pairs. Formation of an ester in the context of separating stereoisomers is a different use from use of an ester as a prodrug.

Applicants note that "prodrugs" are described at page 28, lines 14 to 20. Applicants note that the term "prodrugs" includes esters. Accordingly, Applicants have deleted "esters" from claim 14.

Subparagraph E

Applicants submit that the change in dependency of claim 13 deals appropriately with this rejection.

Conclusion

Applicants request that the Examiner reconsider this rejection in view of their remarks and withdraw it.

The Section 112, First Paragraph Rejection of Paragraph 3

Claims 1 to 5, 8 to 14, 15 to 35, 36 to 39 and 50 to 52 stand rejected under 35 U.S.C. § 112, first paragraph as assertedly non-enabled.

Subparagraph (I) How to Make

The Examiner asserted that the Specification fails to enable preparation of the claimed compounds.

Applicants submit that the Examiner's position is not well taken and that the Specification does enable one of skill in the art to make the compounds of elected Group I.

Applicants note that the claims have been amended to focus on the elected invention of Group I which involves compounds, compositions and methods of use wherein Z is a piperidino group.

With respect to compounds having Ar_1 and Ar_2 groups which are other than substituted phenyl, Applicants submit that using the teachings in the Specification coupled with the level of knowledge of one of skill in the art, and using the appropriate reagents and starting materials, one of skill in the art would be able to synthesize the compounds, as presently claimed after entry of the present amendments, without undue experimentation.

Applicants note that the Examples teach procedures of making the claimed compounds which would be applicable to compounds wherein Ar_1 and Ar_2 are other than substituted phenyl. Applicants note that the appropriate starting materials include aldehyde (Het-CHO), isocyanate (Het-N=C=W), carboxylic acid halide (Het-COX where X is halo), carboxylic anhydride ((Het-C=O)$_2$O), carboxylic acid (Het-COOH) or amino (Het-NH_2) derivatives where Het is hetaroaryl or heteroaralkyl. Some of these derivatives are commercially available (such as 2-benzofurancarboxylic acid, 5-benzimidazolecarboxylic acid, benzotriazole-5-carboxylic acid, 2-pyridinecarboxaldehyde, 3-pyridinecarboxaldehyde, pyrrole-2-carboxaldehyde, pyrrole-2-carboxylic acid, 2-thiophenecarboxylic acid, 3-thiophenecarboxylic acid, 2-pyrazinecarboxylic acid, 4-pyrazolecarboxylic acid). Other starting materials may be

prepared by known and published synthetic procedures which are well within the level of skill in the art.

Applicants note that Examples 70 and 74 describe compounds having one of Ar_1 and Ar_2 other than substituted phenyl.

Applicants submit that the teachings of Specification and claims, as originally filed, coupled with the level of knowledge and skill in the art, clearly would enable one of skill in the art to make the compounds which are the subject of the elected invention of Group I.

Subparagraph II How to Use

The Examiner asserts that the specification fails to enable one of skill in the art to use the claimed compounds.

Applicants submit that the Examiner's position is also not well-taken in this regard and that the uses as presently claimed are clearly enabled.

Applicants note that claims 50 to 52, which were directed to methods of identifying a genetic polymorphism and methods of identifying a subject suitable for treatment by detecting presence of a polymorphism, have been cancelled without prejudice to expedite prosecution. Applicants believe that these claims are clearly enabled and cancellation of these claims should not be construed as acquiescence to the merits of this rejection. Applicants reserve their right to pursue the subject matter in appropriate continuing applications.

With regard to the other method of use claims, Applicants submit that these uses are clearly enabled. Applicants note that they have provided data from a variety of assays and animal models which are deemed reasonably predictive of the claimed *in vivo* utility for a number of compounds which with are within the invention of elected Group I.

Applicants note that the Examiner makes the assertion:

> "All the compounds actually tested are structurally different from the claimed compounds such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the instantly claimed compounds."

Office Action mailed April 25 at page 6. Applicants submit that the Examiner is mistaken and that almost all of the compounds for which data are provided are compounds of elected invention of Group I and, accordingly, are within the claims as presently pending after entry of the amendments presented here. Applicants note Tables 1, 4 and 5 each appear to have data for one (1) compound of non-elected group B or C.

Accordingly, Applicants submit that they have taught how to use the elected invention.

Applicants note the Examiner's citation of M.P.E.P. § 806.05(h) and submit that it does not appear to support the Examiner's position in regard to examination of method claims for one method of use with the elected compounds should this rejection be maintained, clarification is requested.

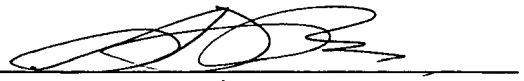
CONCLUSION

In view of the foregoing, Applicants submit that the rejections of claims 1, 2, 4 to 9, 11 to 49 have been overcome and that those claims are allowable. Applicants submit that new claim 53 is also allowable. Applicants request that the claims be allowed and passed to issue.

If the Examiner believes that a telephonic interview would expedite allowance of this application, he is encouraged to telephone Applicant's attorney of record, Suzanne L. Biggs at the below-noted telephone number.

The Commissioner is hereby authorized to charge any fee, including any fee due with this submission, if the attached check(s) is in the wrong amount or otherwise improper or missing, that may be due in connection with this and the attached papers, or with this application during its entire pendency to or to credit any overpayment to Deposit Account 03-3975, Order No. 015185-0272568.

Respectfully submitted,
PILLSBURY WINTHROP LLP

By 
Suzanne L. Biggs
Registration No. 30,158

Dated: August 12, 2002

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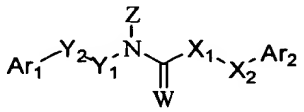
triazole, benzotriazole, pyridine, quionoline, isoquinoline, pyridazine, pyrimidine, purine, pyrazine, pteridine, and triazine. The most preferred substituents are halo, hydroxy, cyano, lower alkoxy, lower alkyl, lower hydroxyalkyl, lower alkylamino, and lower aminoalkyl.

The present invention provides compounds preferably showing a realtively high selectivity toward serotonin receptors, particularly, 5-HT2A receptors, which may have a beneficial effect in the treatment of neuropsychiatric disorders.

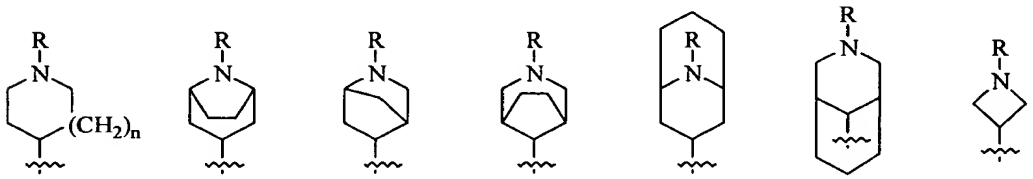
According to one embodiment, the present invention provides compounds of the general formula (I):



I

wherein

Z is



, , , , , or

in which

R is a hydrogen, a cyclic or straight-chained or branched acyclic organyl group, a lower hydroxyalkyl group, a lower aminoalkyl group, or an aralkyl or heteroaralkyl group;

n is 0, 1, or 2;

X_1 is methylene, vinylene,or an NH or N (lower alkyl) group; and

X_2 is methylene , or, when X_1 is methylene or vinylene, X_2 is methylene or a bond; or when X_1 is methylene, X_2 is O, S, NH, or N(lower alkyl) or a bond;

[X]

Y_1 is methylene and Y_2 is methylene, vinylene, ethylene, propylene, or a bond; or

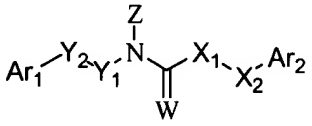
Y_1 is a bond and Y_2 is vinylene; or

Y_1 is ethylene and Y_2 is O, S, NH, or N(lower alkyl);

CLAIMS MARKED UP TO SHOW CHANGES

We Claim:

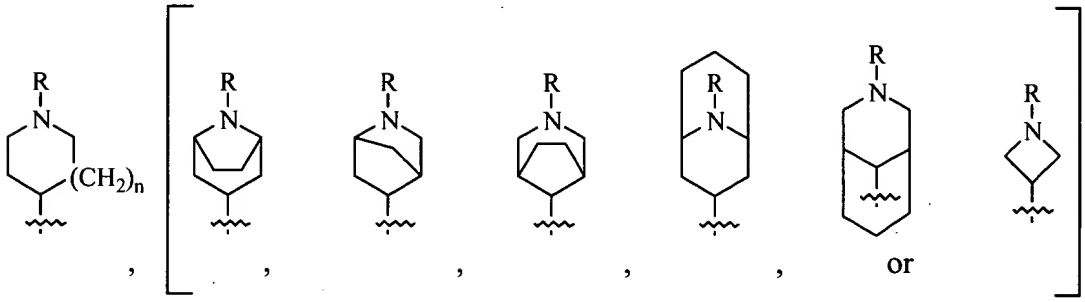
1. (Amended) A compound of formula (I)



I

wherein

Z is



in which

R is a hydrogen, a cyclic or straight-chained or branched acyclic organyl group, a lower hydroxyalkyl group, a lower aminoalkyl group, or an aralkyl or heteroaralkyl group;

n is [0,] 1[, or 2];

X_1 is methylene, vinylene, or an NH or N(lower alkyl) group; and

X_2 is methylene , or, when X_1 is methylene or vinylene, X_2 is methylene or a bond; or when X_1 is methylene, X_2 is O, S, NH, or N(lower alkyl) or a bond;

Y_1 is methylene and Y_2 is methylene, vinylene, ethylene, propylene, or a bond; or

Y_1 is a bond and Y_2 is vinylene; or

Y_1 is ethylene and Y_2 is O, S, NH, or N(lower alkyl);

Ar_1 and Ar_2 independently are unsubstituted or substituted aryl or heteroaryl groups, provided that Ar_1 and Ar_2 are not simultaneously phenyl; and

W is oxygen [or sulfur]; or

a pharmaceutically acceptable salt or prodrug thereof.

2. A compound according to claim 1, wherein

Y_1 is methylene and Y_2 is a bond, methylene, ethylene, or vinylene; or

Y_1 is ethylene and Y_2 is O or S;

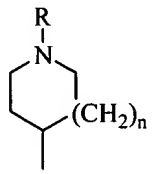
and

X_1 is methylene and X_2 is a bond, methylene, O, or S; or

X_1 is NH or N(lower alkyl) and X_2 is methylene.

[3. A compound according to claim 2, wherein

Z is



and W is oxygen.]

4. (Amended) A compound according to claim [3] 2, wherein

Ar_1 and Ar_2 independently are mono- or disubstituted phenyl groups.

5. A compound according to claim 4, wherein

R is a hydrogen, a lower alkyl group, a cyclic organyl group, or a substituted or unsubstituted aralkyl or heteroaralkyl group;

n is 1;

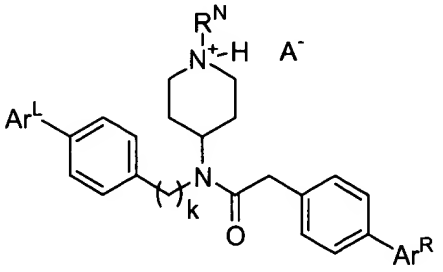
Y_1 is methylene, Y_2 is a bond, methylene, ethylene, or vinylene;

X_1 is methylene and X_2 is a bond, or.

X_1 is NH or N(lower alkyl) and X_2 is methylene; and

Ar_1 and Ar_2 are phenyl groups, independently *p*-substituted with groups selected from lower alkyl, lower alkoxy and halogen.

6. A compound according to claim 1, having a formula (II)



II

wherein R^N is hydrogen, lower alkyl, aralkyl, or heteroaralkyl;

Ar^L is selected from lower alkyl, lower alkoxy and halogen

Ar^R is selected from lower alkyl, lower alkoxy and halogen;

k is 1 or 2

and A^- is a suitable anion.

7. (Amended) The compound according to claim 1, wherein the compound is selected from the group consisting of:

N-(1-(1-methylethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(2,2-dimethylethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-pentylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-hexylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-cyclohexylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-cyclopentylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-cyclobutylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-cyclopropylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(cyclopentylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(cyclobutylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(cyclopropylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(2-hydroxyethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(3-hydroxypropyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-*N*-(piperidin-4-yl)-*N*'-phenylmethylcarbamide;

N-((4-methylphenyl)methyl)-*N*-(1-(2-methylpropyl)piperidin-4-yl)-*N*'-phenylmethylcarbamide;

N-(1-((2-bromophenyl)methyl)piperidin-4-yl)-*N*-((4-methylphenyl)methyl)-*N*'-phenylmethylcarbamide;

N-(1-((4-hydroxy-3-methoxyphenyl)methyl)piperidin-4-yl)-*N*-((4-methylphenyl)methyl)-*N*'-phenylmethylcarbamide;

N-(1-((5-ethylthien-2-yl)methyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-N'-phenylmethylcarbamide;

N-(1-(imidazol-2-ylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-N'-phenylmethylcarbamide;

N-(1-(cyclohexylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-N'-phenylmethylcarbamide;

N-(1-((4-fluorophenyl)methyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-N'-phenylmethylcarbamide;

N-((4-methylphenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-methylpiperidin-4-yl)-4-methoxyphenylacetamide;

N-(1-ethylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-propylpiperidin-4-yl)-4-methoxyphenylacetamide;

N-(1-butylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(3,3-dimethylbutyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(cyclohexylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-(2-methylpropyl)piperidin-4-yl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-((4-methylphenyl)methyl)piperidin-4-yl)-4-methoxyphenylacetamide;

N-(1-((4-hydroxyphenyl)methyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-((2-hydroxyphenyl)methyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(3-phenylpropyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-(2-phenylethyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((2-methoxyphenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((2-chlorophenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((3,4-di-methoxyphenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((4-fluorophenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((2,4-di-chlorophenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((3-methylphenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((3-bromophenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-(1-(phenylmethyl)piperidin-4-yl)-N-(3-phenyl-2-propen-1-yl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-phenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-3-phenylpropionamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-(phenylthio)acetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-phenoxyacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-(4-chlorophenoxy)acetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-3-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-4-fluorophenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-2,5-di-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-4-chlorophenylacetamide;

[N-((4-methylphenyl)methyl)-N-(1-(phenylmethyl)pyrrolidin-3-yl)-N'-phenylmethylcarbamide;

N-((4-methylphenyl)methyl)-N-(1-(phenylmethyl)pyrrolidin-3-yl)-4-methoxyphenylacetamide;]

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-(piperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-(1-ethylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-chlorbenzyl)-*N*-(1-ethylpiperidin-4-yl) acetamide.

2-(4-methoxyphenyl)-*N*-(4-chlorbenzyl)-*N*-(1-isopropylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-chlorobenzyl)-*N*-(piperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-chlorbenzyl)-*N*-(1-cyclopentylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-chlorbenzyl)-*N*-(1-isopropylpiperidin-4-yl) acetamide;

2-(phenyl)-*N*-(4-trifluoromethylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-fluorophenyl)-*N*-(4-trifluoromethylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-*N*-(4-trifluoromethylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Trifluoromethylphenyl)-*N*-(4-trifluoromethylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Fluorophenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(phenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Trifluoromethylphenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-trifluoromethylphenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-Phenyl-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Chlorophenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-trifluoromethylphenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-Phenyl-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Chlorophenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4 methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(4-chloromethyl-2-thiazolylmethyl) piperidin-4-yl] acetamide;

2-(4 methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[3(1,3 dihydro-2H-benzimidazol-2-on-1-yl) propyl] piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(2-4(fluorophenyl) ethyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(2,5-dimethoxyphenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(2,4-dichlorophenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(3-chlorophenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(4-methoxyphenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(3-fluorophenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-ethoxyphenyl)-*N*-[2-(4-fluorophenethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-ethoxyphenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[2-(2-hydroxyethoxy)ethyl] piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-((2-chloro-5-thienyl)methyl) piperidin-4-yl] acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(2-(imidazolidinon-1-yl)ethyl)piperidin-4-yl] acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[2-(2,4(1H,3H)quinazolinedion-3-yl)ethyl] piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[2-(1,3-dioxolan-2-yl)ethyl]piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[2-(3-indolyl)ethyl] piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[3-(1,2,4-triazol-1-yl)propyl]piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(5-benzofurazanylmethyl)piperidin-4-yl] acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(5-chlorobenzo[b]thien-3-ylmethyl) piperidin-4-yl] acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(5-phenyl-1,2,4-oxadiazol-3-ylmethyl)piperidin-4-yl] acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-isopropylpiperidin-4-yl)-acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-ethylpiperidin-4-yl)-acetamide;

2-Phenyl-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide[,2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide];

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-cyclopentylpiperidin-4-yl)-acetamide;

2-(4-Fluorophenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-(2-hydroxyethyl)-piperidin-4-yl)-acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-cyclobutylpiperidin-4-yl)-acetamide;

2-(4-Methoxyphenyl)-N-(4-methylbenzyl)-N-(1-cyclobutylpiperidin-4-yl)-acetamide[,2-(4-Methoxyphenyl)-N-(4-methylbenzyl)-N-(tropin-4-yl)-acetamide];

N-(4-Methylbenzyl)-N-(1-methylpiperidin-4-yl)-N′-benzyl-carbamide;

N-(4-Methylbenzyl)-N-(1-methylpiperidin-4-yl)-N′-phenyl-carbamide;

N-Phenethyl-N-(1-methylpiperidin-4-yl)-N′-benzyl-carbamide;

2-Phenyl-N-(4-methoxybenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Trifluoromethylphenyl)-N-(4-methoxybenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Fluorophenyl)-N-(4-methoxybenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Methoxyphenyl)-N-(4-methoxybenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Methylphenyl)-N-(4-chlorobenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Hydroxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

N-Phenethyl-N-(1-methylpiperidin-4-yl)-N′-phenyl-carbamide;

N-(3-Phenylpropyl)-N-(1-methylpiperidin-4-yl)-N′-benzyl-carbamide;

N-(3-Phenylpropyl)-N-(1-methylpiperidin-4-yl)-N′-phenyl-carbamide;

2-(4-Methoxyphenyl)-2,2-ethylene-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-N-alpha-methylbenzyl-N-(1-methylpiperidin-4-yl) acetamide;

[2-(4-Methoxyphenyl)-N-(4-methylbenzyl)-N-(3-tropen-4-yl) acetamide;]

2-Phenyl-2-ethyl-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

N-Phenethyl-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-amine;

2-(4-Methoxyphenyl)-N-(1-indanyl)-N-(1-methylpiperidin-4-yl) acetamide;

N-(4-Methylbenzyl)-N-(1-methylpiperidin-4-yl)-N′-(4-methoxybenzyl)-carbamide;

2-(3,4-dimethoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(3,4-Methylenedioxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-N-(4-methylbenzyl)-N-(1-t-butylpiperidin-4-yl)-acetamide;

N-(4-Methylbenzyl)-N-(1-methylpiperidin-4-yl)-N′-phenethyl-carbamide;

N-Phenethyl-N-(1-methylpiperidin-4-yl)-N′-phenethyl-carbamide;

N-(4-Methylbenzyl)-N-(1-t-butylpiperidin-4-yl)-N′-(4-methoxybenzyl)-carbamide;

2-(4-Ethoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Butoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-i-Propoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-t-Butoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

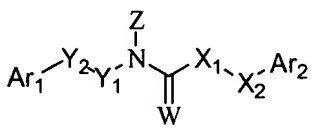
2-(4-Butoxyphenyl)-N-(4-fluorobenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Propoxyphenyl)-N-(4-flourobenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-i-Propoxyphenyl)-N-(4-fluorobenzyl)-N-(1-methylpiperidin-4-yl) acetamide; and

2-(4-t-Butoxyphenyl)-N-(4-fluorobenzyl)-N-(1-methylpiperidin-4-yl) acetamide.

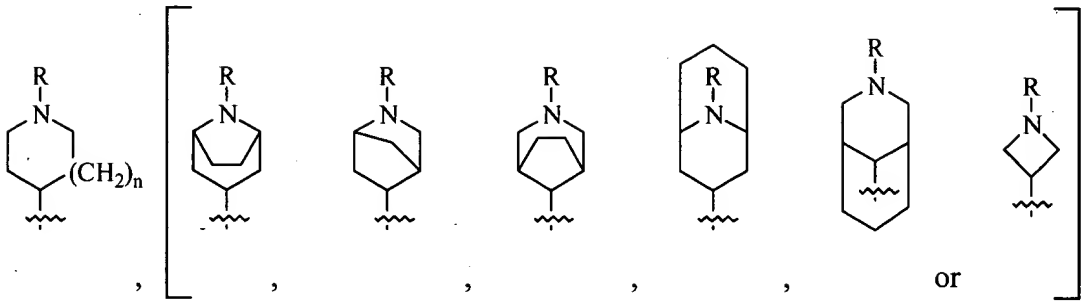
8. (Amended) A compound of formula (I)



I

wherein

Z is



in which

R is a hydrogen, a cyclic or straight-chained or branched acyclic organyl group, a lower hydroxyalkyl group, a lower aminoalkyl group, or an aralkyl or heteroaralkyl group; and

n is [0,] 1[, or 2];

X_1 is methylene, vinylene, or an NH or N(lower alkyl) group; and

X_2 is methylene, or, when X_1 is methylene or vinylene, X_2 is methylene or a bond; or when X_1 is methylene, X_2 is O, S, NH, or N(lower alkyl) or a bond;

Y_1 is methylene and Y_2 is methylene, vinylene, ethylene, propylene, or a bond; or

Y_1 is a bond and Y_2 is vinylene; or

Y_1 is ethylene and Y_2 is O, S, NH, or N(lower alkyl);

Ar_1 and Ar_2 are different unsubstituted or substituted aryl or heteroaryl groups; and

W is oxygen[or sulfur]; or

a pharmaceutically acceptable salt or prodrug thereof.

9. A compound according to claim 8, wherein

Y_1 is methylene and Y_2 is a bond, methylene, ethylene, or vinylene; or

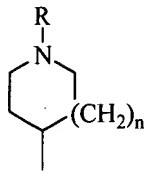
Y_1 is ethylene and Y_2 is O or S; and

X_1 is methylene and X_2 is a bond, methylene, O, or S; or

X_1 is NH or N(lower alkyl) and X_2 is a methylene .

[10. A compound according to claim 9, wherein

Z is



and W is oxygen.]

11. (Amended) A compound according to claim [10]9, wherein

Ar_1 and Ar_2 independently are mono- or disubstituted phenyl groups.

12. (Amended) A compound according to claim 11, wherein

R is a hydrogen, a lower alkyl group, a cyclic organyl group, or an, optionally substituted, alalkyl or heteroaralkyl group;

[n is 1;]

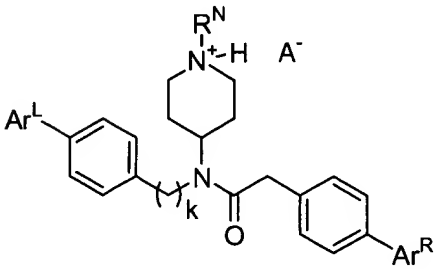
Y_1 is methylene, Y_2 is a bond, methylene, ethylene, or vinylene;

X_1 is methylene and X_2 is a bond, or

X_1 is NH or N(lower alkyl) and X_2 is methylene; and

Ar_1 and Ar_2 are phenyl groups, independently p-substituted with groups selected from alkyl, lower alkoxy and halogen.

13. (Amended) A compound according to claim [7]8, having a formula (II):



II

wherein R^N is hydrogen, lower alkyl, aralkyl, or heteroaralkyl;

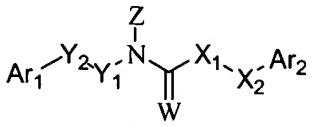
Ar^L is selected from lower alkyl, lower alkoxy and halogen

Ar^R is selected from lower alkyl, lower alkoxy and halogen;

k is 1 or 2

and A^- is a suitable anion.

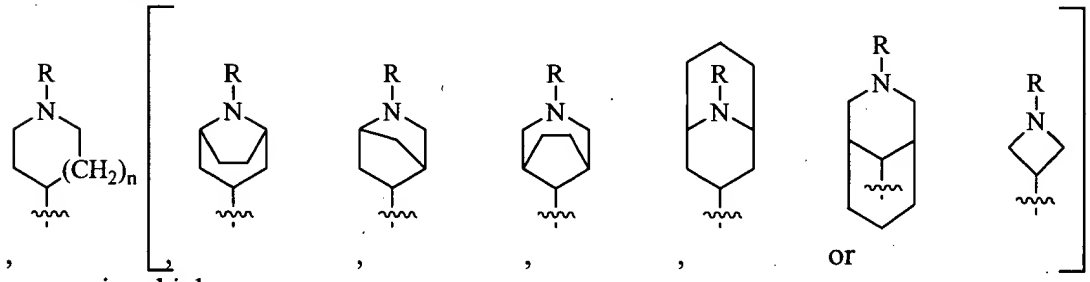
14. (Amended) A pharmaceutical composition comprising an effective amount of a compound of formula (I):



I

wherein

Z is



in which

R is a hydrogen, a cyclic or straight-chained or branched acyclic organyl group, a lower hydroxyalkyl group, a lower aminoalkyl group, or an aralkyl or heteroaralkyl group; and

n is [0,] 1[, or 2];

X_1 is methylene, vinylene, or an NH or N(lower alkyl) group; and

X_2 is methylene, or, when X_1 is methylene or vinylene, X_2 is methylene or a bond; or when X_1 is methylene, X_2 is O, S, NH, or N(lower alkyl) or a bond;

Y_1 is methylene and Y_2 is methylene, vinylene, ethylene, propylene, or a bond; or

Y_1 is a bond and Y_2 is vinylene; or

Y_1 is ethylene and Y_2 is O, S, NH, or N(lower alkyl);

Ar_1 and Ar_2 independently are unsubstituted or substituted aryl or heteroaryl groups, provided that Ar_1 and Ar_2 are not simultaneously phenyl; and

W is oxygen[or sulfur];

or a pharmaceutically acceptable salt[, ester] or prodrug thereof, and

a pharmaceutically acceptable diluent or excipient.

15. A method of inhibiting an activity of a monoamine receptor comprising contacting the monoamine receptor or a system containing the monoamine receptor with an amount of one or more of the compounds of claim 1 that is effective in inhibiting the activity of the monoamine receptor.

16. The method of claim 15 wherein the monoamine receptor is a serotonin receptor.

17. The method of claim 16 wherein the serotonin receptor is the 5-HT2A subclass.

18. The method of claim 16 wherein the serotonin receptor is in the central nervous system.

19. The method of claim 16 wherein the serotonin receptor is in the peripheral nervous system.

20. The method of claim 16 wherein the serotonin receptor is in blood cells or platelets.

21. The method of claim 16 wherein the serotonin receptor is mutated or modified.

22. The method of claim 15 wherein the activity is signaling activity.

23. The method of claim 15 wherein the activity is constitutive.

24. The method of claim 15 wherein the activity is associated with serotonin receptor activation.

25. A method of inhibiting an activation of a monoamine receptor comprising contacting the monoamine receptor or a system containing the monoamine receptor with an amount of a compound of one or more of the compounds of claim 1 that is effective in inhibiting the activation of the monoamine receptor.

26. The method of claim 25 wherein the activation is by an agonistic agent.

27. The method of claim 26 wherein the agonistic agent is exogenous.

28. The method of claim 26 wherein the agonistic agent is endogenous.

29. The method of claim 25 wherein the activation is constitutive.

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30. The method of claim 25 wherein the monoamine receptor is a serotonin receptor.

31. The method of claim 30 wherein the serotonin receptor is the 5-HT2A subclass.

32. The method of claim 30 wherein the serotonin receptor is in the central nervous system.

33. The method of claim 30 wherein the serotonin receptor is in the peripheral nervous system.

34. The method of claim 30 wherein the serotonin receptor is in blood cells or platelets.

35. The method of claim 30 wherein the serotonin receptor is mutated or modified.

36. A method of treating a disease condition associated with a monoamine receptor comprising administering to a subject in need of such treatment a therapeutically effective amount of one or more of the compounds of claim 1.

37. The method of claim 36 wherein the disease condition is selected from the group consisting of schizophrenia, psychosis, migraine, hypertension, thrombosis, vasospasm, ischemia, depression, anxiety, sleep disorders and appetite disorders.

38. The method of claim 36 wherein the disease condition is associated with dysfunction of a monoamine receptor.

39. The method of claim 36 wherein the disease condition is associated with activation of a monoamine receptor.

40. The method of claim 36 wherein the disease condition is associated with increased activity of monoamine receptor.

41. The method of claim 36 wherein the monoamine receptor is a serotonin receptor

42. The method of claim 41 wherein the serotonin receptor is the 5-HT2A subclass.

43. The method of claim 41 wherein the serotonin receptor is in the central nervous system.

44. The method of claim 41 wherein the serotonin receptor is in the peripheral nervous system.

45. The method of claim 41 wherein the serotonin receptor is in blood cells or platelets.

46. The method of claim 41 wherein the serotonin receptor is mutated or modified.

47. A method of treating schizophrenia comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of one or more of the compounds of claim 1.

48. A method of treating migraine comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of one or more of the compounds of claim 1.

49. A method of treating psychosis comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of one or more of the compounds of claim 1.

[50. A method for identifying a genetic polymorphism predisposing a subject to being responsive to one or more of the compounds of claim 1, comprising:

administering to a subject a therapeutically effective amount of the compound;

measuring the response of said subject to said compound, thereby identifying a responsive subject having an ameliorated disease condition associated with a monoamine receptor; and

identifying a genetic polymorphism in the responsive subject, wherein the genetic polymorphism predisposes a subject to being responsive to the compound.

51. The method of claim 50 wherein the ameliorated disease condition is associated with the 5-HT class or 5-HT2A subclass of monoaminergic receptors.

52. A method for identifying a subject suitable for treatment with one or more of the compounds of claim 1, comprising detecting the presence of a polymorphism in a subject wherein the polymorphism predisposes the subject to being responsive to the compound, and wherein the presence of the polymorphism indicates that the subject is suitable for treatment with one or more of the compounds of claim 1.]

53. (New) A method according to claim 49 wherein the psychosis is a drug-induced psychosis.

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